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EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
09/17/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/566,402	TORRENS JOVER ET AL.	
	Examiner	Art Unit	
	UMAMAHESWARI RAMACHANDRAN	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 34-74* is/are pending in the application.

4a) Of the above claim(s) *3 and 48-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-7 and 34-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The office acknowledges the receipt of the amendments, arguments and remarks received on 7/29/2010. Claims 1-7, 34-45 have been amended, claims 8-33 has been cancelled and claims 46-74 have been added new. Applicants elected regulation of appetite as the disease (Response to Restriction/Election dated 1/4/2010). Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 48-74 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP 821.03. Claims 1-7, 34-74 are pending, claims 3, 48-74 are withdrawn from consideration. Claims 1-2, 4-7, 34-47 will be examined on the merits herein.

Response to Remarks

Applicants request that the double patenting rejection be held in abeyance and hence the rejection is maintained and the modified rejection is given based on the amendments of the claims. Applicants' amendment of claims necessitated the withdrawal of rejection of claims 1-2, 4-9 under 35 U.S.C. 112, second paragraph, rejection of claims 1-2, 4-9, 34-45 under 35 U.S.C. 112, first paragraph. The claim objections are withdrawn due to amendment of claims by the Applicants. Claims 8-9 rejected under 35 U.S.C. 101 and 112(2) are withdrawn due to cancellation of claims by the Applicants. Applicants' arguments regarding the 112(1) and 103 rejections have been fully considered but found not to be persuasive. The rejections are addressed in the response to arguments section below. Applicants' amendment of claims

necessitated the modified rejections presented in this action. Accordingly, the action is made Final.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 4-7, 34-47 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 4-9, 34-45 of copending Application No. 10/566,100.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant application and the co-pending application teach an active substance combination of at least one compound with neuropeptide receptor Y (NPY) affinity and at least one compound with 5-HT6 receptor affinity or formulation comprising the same or method of simultaneously regulating neuropeptide

Y5 and 5-HT6 receptor with an effective amount of the active substance combination of claim 1 or 2.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-7, 34-47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to an active substance combination of at least one compound with neuropeptide receptor Y (NPY) affinity and at least one compound with 5-HT6 receptor affinity or formulation comprising the same or method of simultaneously regulating neuropeptide Y5 and 5-HT6 receptor comprising administering to a subject an effective amount of the active substance combination of claim 1 or 2. The claims are very broad in scope with respect to the number of compounds in combination, in preparation of the pharmaceutical formulation and use of such combination in method of regulation of the receptors neuropeptide Y and 5-HT6. As shown in the specification (p 285, lines 10-25) regulation of neuropeptide Y5 and 5-HT6 receptor includes regulation of appetite, maintenance, increase or

reduction of body weight, prophylaxis and/or treatment of disorders related to food ingestion, preferably for prophylaxis and/or treatment of obesity, anorexia, cachexia, bulimia, diabetes, preferably type II diabetes (non-insulin-dependent diabetes mellitus), or prophylaxis and/or treatment of gastrointestinal tract disorders, preferably of the irritable bowel syndrome, prophylaxis and/or treatment of Peripheral Nervous System Disorders, Central Nervous System Disorders, arthritis, epilepsy, anxiety, panic, depression, cognitive disorders, memory disorders, cardiovascular diseases, senile dementia processes, such as Alzheimer's, Parkinson's and/or Huntington's Disease, schizophrenia, psychosis, infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder), pain, hypertensive syndrome, inflammatoric diseases, immunologic !5 diseases or for improvement of cognition etc. As it can be seen the regulation of neuropeptide Y5 and 5-HT6 receptor is involved in a multitude of diseases and each disease has a different and distinct etiology and pathophysiological manifestations, and that each is differently treated. The various individual compounds that have receptor affinity for neuropeptide Y and 5-HT6 receptor affinity are different compounds with different structures imparting highly diverse physical and chemical properties, bioavailabilites, receptor affinities, pharmacokinetic profiles, and treatment efficacies. Applicants have claimed a combination of at least one compound with neuropeptide Y affinity and at least one compound with 5-HT6 receptor affinity and a method of regulating neuropeptide Y5 and 5-HT6 receptor using such active combination.

The specification provides guidance to synthesis of some of the compounds that bind to NPY receptor and binding results for some of the representative compounds of

formula (Ia-Ih) to NPY receptor and 5-HT6 receptor. If the active agents claimed are in a single pharmaceutical formulation then a person of ordinary skill in the art has to do an undue experimentation to prepare such a combination with the active substances claimed and test in combination therapy for potential drug interactions, toxicity measurements etc. Applicants' have claimed the same active substance combination for treating various diverse disorders such as bulimia and anorexia. It is not predictable from the guidance given by the Applicants' (synthesis of some of the compounds with NPY receptor affinity and binding affinity for some representative samples of the compounds synthesized) that the same formulation would be useful for treating obesity and bulimia. It is not predictable from the guidance given by the Applicants' that the same pharmaceutical formulation manufactured will be useful for treating cardiovascular disorders and Alzheimer's when neuropeptide Y and 5-HT6 receptors are regulated. Since the regulation of neuropeptide Y and 5-HT6 receptors involves various disorders and each disease has a different and distinct etiology and pathophysiological manifestations. It is not predictable from the art or from specification that every single active substance combination which can contain one or more (or several) compound (s) with neuropeptide Y receptor affinity and one or more (or several) compound (s) with HT-6 receptor affinity will be useful in regulating the neuropeptide Y receptor and 5-HT6 receptor simultaneously. It would be an undue experimentation to a person of ordinary skill in the art to find the right amount of one or more (or several) compound (s) with neuropeptide Y receptor affinity and one or more (or several) compound (s) with HT-6 receptor affinity to find whether it regulates neuropeptide Y receptor and 5-HT6 receptor

simultaneously. Applicants have claimed a large number of compounds and there are at least six different receptor subtypes named Y1-Y6 in NPY binding receptor family, each NPY receptor subtype is generally associated to a different biological activity. There are a large number of agonists, antagonist compounds that fall under the category of 5-HT6 receptor affinity compounds. Applicants' have not provided any guidance to making any of the pharmaceutical compositions with active substances in combination and using them in regulation of neuropeptide Y receptor and 5-HT6 receptor simultaneously or in the regulation of appetite. It is not clear from the specification whether any amount of active substance that has neuropeptide receptor affinity in combination with any amount of a compound that has 5-HT6 receptor affinity will simultaneously regulate neuropeptide Y and 5-HT6 receptor. It is not predictable from the art or from specification that every single active substance combination which can contain one or more (or several) compound (s) with neuropeptide Y receptor affinity and one or more (or several) compound (s) with HT-6 receptor affinity will be useful in regulating the appetite disorder. A skilled artisan would not recognize that Applicants' were in possession of the claimed invention, of using such an active combination of one or more (or several) compound (s) with neuropeptide Y receptor affinity and one or more (or several) compound (s) with HT-6 receptor affinity in regulation of neuropeptide Y and 5-HT6 receptor or in regulation of a disorder such as appetite in using such active substance combinations.

Claim Rejections - 35 USC § 103

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 4-7, 34-37, 46-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bruns (U.S. 5,567,714) in view of Merce-Vidal et al. (U.S. 7,105,515, effective filing date Nov 13 2002) and Caldirola et al. (U.S. 7,144,883, effective filing date, June 11 2002).

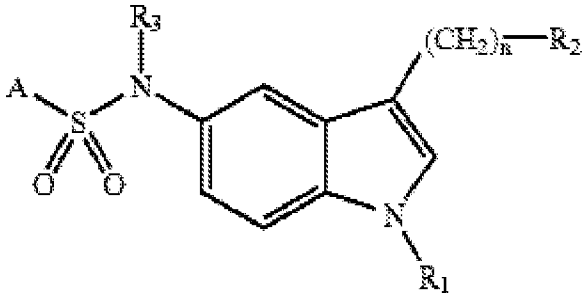
Bruns teaches a method of inhibiting a physiological disorder associated with an excess of neuropeptide Y such as disorders pertaining to the heart, obesity, diseases related to the CNS such as neurodegenerative conditions etc administering

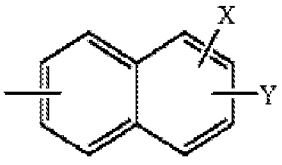
neuropeptide Y receptor antagonists (See abstract, col. 9, lines 40-65, col. 10, claim 1). The reference describes formulation of the neuropeptide Y compounds (col. 5, 6) and the use of such compounds in a method of treatment in a dosage amount of 5 mg (capsule) to 1000 mg (suspension) (see col. 10, claims 1-4). Bruns teaches pharmaceutical formulations comprising NPY affinity compounds as capsules, tablets, suspensions etc for oral administration. The reference also teaches that the pharmaceutical formulation is present in the form of granules then compacted to a tablet (col. 6, lines 25-34).

The reference does not teach a combination of the active neuropeptide Y receptor affinity compound with a HT-6 receptor affinity compound.

The reference Merce-Vidal teaches derivatives of sulphonamides (see abstract).

(I)



When R1=H, n=0, A= 

, R3=H the reference teaches the elected species for 5-HT6 (see col. 2, lines 50, 65, 67, col. 3, line 24). The reference provides guidance towards the synthesis of the sulfonamide compounds, its pharmaceutical formulation the amount of daily doses (1-500 mg) in human medicine

(see col. 33, lines 55-67, col. 34, example 1). Merce-Vidal teaches that the compounds have 5-HT6 serotonin receptor antagonistic activity useful in the preparation of medicament for prevention or treatment of various CNS (central nervous system) disorders.

Caldirola et al. teaches substituted sulfonamide compounds with 5-HT6 receptor affinity to be useful for the prophylaxis and treatment of medical conditions relating to obesity, type II diabetes and/or disorders of the central nervous system (see abstract, col. 2, lines 31-35). The reference teaches preparation of such compounds, pharmaceutical formulations and a method of using such compounds in treating obesity (col. 107, claims 7-9).

It would have been obvious to one having ordinary skill in the art at the time of the invention to have combined a compound with neuropeptide receptor affinity with that of a compound with 5-HT6 serotonin receptor affinity from the teachings of Bruns and Merce-Vidal. Bruns teaches the use of NPY affinity compounds to be useful in treating CNS disorders and Merce-Vidal teaches the use of 5-HT6 receptor binding compounds to be useful in CNS disorders. It would have been obvious to one having ordinary skill in the art at the time of the invention to have made a combination or a formulation or a medicament of at least one compound with NPY receptor affinity with at least one compound with 5-HT6 receptor affinity because both of them have been taught in the prior art to be useful in a method of treating CNS disorders. One having ordinary skill in the art would have been motivated in making such a medicament combination in expectation of using the same in a method of treating CNS disorders. One of ordinary

skill in the art would have been motivated to incorporate the two agents herein in a single combination pharmaceutical composition because combining the agents herein each of which is known to be useful to treat a disorder individually into a single composition useful for the very same purpose is *prima facie* obvious. See *In re Kerkhoven* 205 USPQ 1069. It would have been obvious to one having ordinary skill in the art at the time of the invention to have manufactured a pharmaceutical composition combining NPY receptor affinity compound with 5HT-6 receptor affinity compound to use in regulation of appetite because the prior art shown above teaches the preparation of pharmaceutical formulations of the active formulations and their use in treating obesity. Obesity is an eating disorder and one of the root causes for obesity is excessive consumption of food. Appetite is a desire to eat food when hungry and abnormal appetite could lead to an eating disorder, obesity. Hence treating obesity condition leads to suppression of appetite or regulation of appetite. It would have been obvious to one having ordinary skill in the art at the time of the invention to have made a formulation of an active substance combination comprising one or more compounds with neuropeptide receptor affinity with that of one or more compounds with 5-HT6 serotonin receptor affinity or use such formulation in neuropeptide Y5 and 5-HT6 regulation and regulate appetite. It would have been obvious to a person of ordinary skill in the art to use such combination in a method of regulating the receptors (NPY-5 and 5-HT6) and regulate appetite disorder from the teachings of prior art. A person of ordinary skill in the art would have been motivated to do so in order to attain therapeutic benefits in treating disorders such as obesity. The references do not explicitly teach the

percent weight amounts of NPY receptor affinity compound and 5-HT6 receptor affinity compound for active substance combination. However, the references in general teach dosage amounts of NPY receptor affinity compound and 5-HT6 receptor affinity compounds in making formulations. It would have been obvious to one of ordinary skill in the art at the time of the invention to have adjusted the amounts of component A and component B as claimed by the Applicants (claim 5) through routine experimental procedure. Generally, the ratios of concentration will not support the patentability unless there is evidence indicating such concentration is critical. "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233, 235 (CCPA 1955).

Claims 38-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bruns (U.S. 5,567,714) in view of Merce-Vidal et al. (U.S. 7,105,515, effective filing date Nov 13 2002) and Caldirola et al. (U.S. 7,144,883, effective filing date, June 11 2002) as applied to claims above and further in view of Noda et al. (U.S. 5,320,853).

Bruns, Merce-Vidal et al. and Caldirola et al teachings discussed as above.

The references do not teach the pharmaceutical formulation in a sustained release form.

Noda et al. teaches controlled release formulation for pharmaceutical compounds. The reference teaches a coat and sustainable drug releasing exterior coat (see Abstract). The reference teaches water insoluble polymers including ethylcellulose, cellulose acetate (col.2, lines 40-45), drug releasing polymers such as acrylates and/or

methacrylates (Eudagrit) (col. 5, lines 10-20, col. 6, lines 55-65), plasticizers (col. 5, lines 37-40) and white wax (also known as beeswax) (col. 9, line 8) in the sustained release formulation.

It would have been obvious to one having ordinary skill in the art at the time of the invention to have combined a compound with neuropeptide receptor affinity with that of a compound with 5-HT6 serotonin receptor affinity and make a controlled release drug delivery device comprising such combination because it within the knowledge of the skilled pharmacologist and represent conventional formulations and modes of administration. It is well known from the prior art teachings like Noda et al. that such conventional formulations can be made. One having ordinary skill in the art at the time of the invention would have been motivated to make a controlled release formulation of the active substance combination claimed in order for once or twice a day administration of the drugs and achieve desired blood levels of the drugs in a manner which delays or sustains the release of the drug. It would have been obvious to one having ordinary skill in the art to formulate a composition where one of the components (A) or (B) as claimed is in a non-sustained release dosage form is in case of a medical condition where one of the components needs to be delivered without any controlled drug delivery.

Response to Arguments

(1) 112(1) rejection:

Applicants argue that the specification provides a detailed teaching regarding how to prepare the combination set forth in Claim 1 and how to administer the combination to treat all of conditions set forth in the claims and accordingly, one skilled in the art reading the present specification would appreciate that the present application provides an adequate written description of the invention.

In response, the claims are directed to an active substance combination of at least one compound with neuropeptide receptor Y (NPY) affinity and at least one compound with 5-HT6 receptor affinity or formulation comprising the same or method of simultaneously regulating neuropeptide Y5 and 5-HT6 receptor comprising administering to a subject an effective amount of the active substance combination of claim 1 or 2. The claims are very broad in scope with respect to the number of compounds in combination, in preparation of the pharmaceutical formulation and use of such combination in method of regulation of the receptors neuropeptide Y and 5-HT6. As shown in the specification (p 285, lines 10-25) regulation of neuropeptide Y5 and 5-HT6 receptor includes regulation and treatment of a variety of unrelated disorders such as Alzheimer's and cardiovascular disorders or obesity. As it can be seen the regulation of neuropeptide Y5 and 5-HT6 receptor is involved in a multitude of diseases and each disease has a different and distinct etiology and pathophysiological manifestations, and that each is differently treated. The various individual compounds that have receptor affinity for neuropeptide Y and 5-HT6 receptor are different compounds with different structures imparting highly diverse physical and chemical properties, bioavailabilites, receptor affinities, pharmacokinetic profiles, and treatment efficacies. Applicants have

not provided a single example of active substance combination of the claimed agents or the use of such combination for regulation of neuropeptide Y and 5-HT6 receptors simultaneously. In such case, a person of ordinary skill in the art has to first envision which combinations will be active in regulation of neuropeptide Y and 5-HT6 receptors together and further have to envision formulation, dosage, duration, route and an appropriate animal model system to test the agent for regulation of a disorder such as appetite. If unsuccessful, one of ordinary skill in the art would have to envision a modification in the formulation, dosage, duration, route of administration etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention of using an active combination comprising at least one compound with neuropeptide receptor Y (NPY) affinity and at least one compound with 5-HT6 receptor affinity for regulation of neuropeptide receptor Y and 5-HT6 receptor simultaneously. It would be an undue experimentation to make such combinations first, find which one is active for regulation of neuropeptide receptor Y and 5-HT6 receptor simultaneously and then test for regulation of the receptors (NPY 5 and 5-HT6) or appetite because the active substance combination involves numerous combinations of compounds with neuropeptide receptor Y (NPY) compounds with compounds of 5-HT6 receptor affinity. Applicants have not described in the specification of which combination of neuropeptide receptor Y (NPY 5) affinity and 5-HT6 receptor affinity will be therapeutically effective in regulation of neuropeptide receptor Y (NPY 5) and 5-HT6 receptor simultaneously or in the regulation of appetite. Applicants have not

described in the specification at what concentrations or dosage amounts such combination will be therapeutically effective because Applicants claim at least one (hence it can be several) compound of neuropeptide receptor Y (NPY 5) affinity and at least one (hence it can be several) compound of 5-HT6 receptor affinity as active substance combination. In order to practice the full scope of the invention, one of ordinary skill in the art would not only need to create synthetic procedures de novo, but also decide what compounds to prepare, and which compounds need to used in combination based on the activity. The long list of the various optional groups includes very large groups, many basic and polar moieties and these modifications may not lead to compounds that maintain utility. Even making the full scope of the compounds is undue experimentation. In the development of Neuropeptide Y ligands which also posses a piperidine core, which is that of the instant case, Jablonowski, J.A. et al. Bioorganic and Medicinal Chemistry Letters 2004, 14, 1239-1242, described the results of making such changes: "This portion of the molecule also appeared to be sensitive to subtle changes in electronics, which were exemplified by significant differences in activity for compounds bearing the 2-pyridyl (27), 3-pyridyl (28) and 4-pyridyl (29) substitution. The 2- and 3-pyridyl analogues retain only minimal activity at the NPY Y2 receptor, while the 4-pyridyl binds modestly with IC50=12 mM. Oxidation of analogue 29 provided the 4- pyridyl-N-oxide analogue 30, which was inactive. Slight activity was also seen in the compound with 2-imidazolyl substitution as shown in analogue 31 ." It is clear that the ability of these compounds to bind an NPY receptor, is highly unpredictable, and that such changes result in compounds that not only have reduced

activity but actually do not have this activity all, which Jablonowski describes as inactive. Hence not all the piperidine compounds may be active and can regulate the neuropeptide Y5 receptor. It would be such as arduous and daunting task to find the effective combination of the active substances and then find the right dosage, duration, route etc for administration to patients to regulate or treat the disorders. It would be an undue experimentation to a person of ordinary skill in the art to practice the claimed invention.

(2) 103(a) rejection:

Applicants' argue that the examiner has failed to establish the case that a combination as the one disclosed in the patent application would be obvious in view of the cited references.

In response, as stated above in the rejection, Bruns teaches a method of treating disorders such as CNS disorders, obesity etc administering neuropeptide Y receptor antagonists. The reference fails to teach a combination neuropeptide Y receptor affinity compound with a HT-6 receptor affinity compound. However Merce-Vidal teaches derivatives of sulphonamides have 5-HT6 serotonin receptor antagonistic activity useful in the treatment of various CNS disorders. Caldirola et al. teaches substituted sulfonamide compounds with 5-HT6 receptor affinity to be useful for the prophylaxis and treatment of medical conditions relating to obesity, type II diabetes and/or disorders of the central nervous system. The reference teaches preparation of such compounds, pharmaceutical formulations and a method of using such compounds in treating obesity. One of ordinary skill in the art would have been motivated to incorporate the two agents

herein in a single combination pharmaceutical composition because combining the agents herein each of which is known to be useful to treat a disorder (e.g CNS disorder or obesity) individually into a single composition useful for the very same purpose is *prima facie* obvious. See *In re Kerkhoven* 205 USPQ 1069. It would have been obvious to one having ordinary skill in the art at the time of the invention to have made a combination or a formulation or a medicament of at least one compound with NPY receptor affinity with at least one compound with 5-HT6 receptor affinity because both of them have been taught in the prior art to be useful in a method of treating CNS disorders. Hence the prior art teachings suggest and there is a strong motivation to combine two agents known for treating a disorder into a single formulation.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the modified rejections presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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